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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/319,521	06/04/1999	MARK F. PITTENGER	640100-326	3211

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/319,521	PITTENGER ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *60 - 99* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60 - 99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. The **examiner** of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Michail Belyavskyi, Group Art Unit 1644, Technology Center 1600

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/22/04 has been entered.

Claims 60 - 99 are pending.

Claims 60-99 are under consideration in the instant application.

In view of the amendment, filed 09/22/04 the following rejections remain:

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless --
(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 37(c) of this title before the invention thereof by the applicant for patent.

4. Claims 60-79 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 5,908,784 as evidenced by Cellgro catalog and newly cited US Biological Cataloge (2004) and Williams et al.

The US Patent 784 teaches a process for producing chondrocytes from mesenchymal stem cells and a process for inducing chondrogenesis in mesenchymal stem cells comprising culturing human mesenchymal stem cells in vitro in a three dimensional format with at least one chondroinductive agent. US Patent '784 teaches that any serum-free animal medium can be used, including DMEM, IMEM, Mc Coy5A and BGJ_b medium (see column 4, lines 25-35 in particlular). The mesenchymal stem cells are preferably isolated, culture expanded human mesenchymal stem cells in a chemically defined serum free environment and are

condensed in close proximity, such as in the form of a three - dimensional cell mass, e.g. packed cells or a centrifugal pellet or in a ceramic cube. The chondroinductive agent is preferably selected, individually or in combination from the group consisting of: 1) a glucocorticoid such as dexamethasone; ii) a member of the transforming growth factor beta super family (TGF –β) such as BMP-2 or BMP-4, TGF-β1; iii) a component of the collagenous extracellular matrix such as collagen 1; and IV) a vitamin A analog such as retinoic acid. Particularly preferred is the combination of dexamethasone and TGF-beta-1, (see entire patent, especially column 2, lines 5-33, and column 9, lines 45-50).

As evidence by Cellgro Catalog and newly cited US Biological Catalog and Williams et al., the glucose content in DMEM, IMEM, Mc Coy5A is about 4.5 g/l. Said concentration is a species of genus glucose concentration from about 3 g/l to about 7 g/l as claimed in claims 60-79. Moreover, as is evidenced by Williams et al., one skilled in the art at the time the invention was made would know that a chondrogenic medium consists of high –glucose Dulbecco's modified Eagle's medium (DMEM) (see entire documenr, page 681 in particular).

A species will anticipate a claim to a genus. See MPEP 2131.02.

The reference teaching anticipates the claimed invention.

Applicant's arguments, filed 09/22/04 have been fully considered, but have not been found convincing.

Applicant asserts that : (i) US Patent '784 does not disclosed or suggest a chondrogenic medium that includes a simple sugar, i.e. glucose in an amount of from about 3 g/l to about 7 g/l. The only concentration of glucose disclosed by US Patent '784 is 1 g/l, which is DMEM-LG, i.e. medium with low glucose; (ii) Cellgro web page does not provide any suggestion or motivation to one of ordinary skill in the art as to the types of cells which may be cultured in DMEM medium.

Contrary to Applicant's assertions, it is noted that US Patent '784 does not disclosed DMEM-LG medium, i.e. medium with low glucose concentration. Applicant's attention is respectively drawn to column 4, lines 25-35 where it is explicitly stated that any serum-free animal medium can be used, including DMEM, IMEM, Mc Coy5A and BGJ_b medium. One skilled in the art would immediately recognized said medium as medium with high glucose content not as medium with low glucose content, as is evidenced by Cellgro catalog and US Biological Cataloge (2004) and Williams et al. It is also noted that in the previous Office Action, mailed 04/22/04 , claims 60-79 were rejected under 35 U.S.C. 102(e). Cellgro referenced was used as evidential reference to support the Examiner position. Thus , said reference should not provide any suggestion or motivation to one of ordinary skill in the art and should not be considered as a secondary reference.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 80- 99 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,908,784 as evidenced by Cellgro catalog and newly cited US Biological Cataloge (2004) and Williams et al., in view of US Patent 5,368,858.

The teaching of US Patent 5,908,784, Cellgro catalog , US Biological Cataloge (2004) and Williams et al., have been discussed, supra.

The US Patent '784, Cellgro catalog , US Biological Cataloge (2004) and Williams et al. does not explicitly teach the use of TGF-β3.

US Patent '858 teaches the use of TGF-β3 in a method of proliferating chondrocytes and states that the activity among members of the TGF-β family are similar (see entire patent including colllmn 8, 1ines7-24). US Patent '784 also teaches that mesenchymal cells when exposed to TGF-β3 will be transformed into a chondrocytes (see entire patent, including column 5, lines 28-33 and 59-67, and claim 1). US Patent '858 also teaches that dosages of 2-10 ng/ml of TGF-β3 (see entire patent, column 18 and claim 1 in particular)

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of US Patent ' 858 to those of US Patent 784 to obtain a claimed process for producing chondrocytes from mesenchymal stem cells using TGF-β3 as one of the chondrioinductive agent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because the activity among members of the TGF-β family are similar, that TGF-β3 can be used in a method of proliferating chondrocytes, and that mesenchymal cells when exposed to TGF-β3 will be transformed into a chondrocytes as taught by US Patent 858. Thus one member of TGF-β family, i.e. TGF-β1 can be substituted for other member of TGF-β family, i.e TGF-β3 in a process for producing chondrocytes from mesenchymal stem cells taught by US Patent '784. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments, filed 09/22/04 have been fully considered, but have not been found convincing.

Applicant Asserts that at best the combination of US Patent '784 and US Patent '858 would suggest to one of ordinary skill in the art to supply a TGF-β3 to a chondrogenic medium which includes glucose at concentration only 1g/l, which is not the Applicant invention. The combined references do not suggest a chondrogenic medium which includes glucose at concentration from about 3 g/l to about 7 g/l.

Contrary to Applicant's assertion, as has been discussed supra, it is the examiner position that the chondrogenic medium taught by US Patent '784 inherently includes glucose at concentration about 4.5 g/l, that is a species of a genus of glucose concentration from about 3 g/l to about 7 g/l as claimed in the instant application.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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November 24, 2004

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